Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

REMARKS

Applicants respectfully bring to the Examiner's attention an error in the communication of the Office Action of July 17, 2002 in which claims 11-16 and 21-24 are listed as pending. Claims 11-16 and 21-24 were canceled by Applicants in their Response to Office Action submitted April 26, 2002.

Amendments

Claim 25 has been canceled without prejudice or disclaimer and not for reasons related to patentablility. Claim 26, which depended from canceled claim 25, has been amended to depend from claim 1. Claim 1 b) has been amended to include the identification of a functional limitation of SEQ ID NO:1, in order to expedite prosecution and not for reasons related to patentability, Applicants have amended Claim 1 b) to read, "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the sequence of SEQ ID NO:1 over the entire length of SEQ ID NO:1, said polypeptide having serine protease activity." Support for this amendment may be found throughout the specification, for example, page 1, lines 16-23 in which amino acid residues H_{65}, D_{120}, and S_{213} in PSA, a serine protease of the kallikrein family, were identified as essential for serine protease activity, and page 11, lines 10-12 in which the same conserved residues critical for serine protease activity, H_{65}, D_{113}, and S_{206}, are identified in SEQ ID NO:1 (HPAK). Applicants respectfully request entry of the amendment.

Applicants have shown in the Response filed October 17, 2002 and in the alignment faxed to Examiner Davis on January 13, 2003, that HPAK shares homology with the kallikrein polypeptide family, a family consisting of members known to have undisputed utility, and therefore, homology can be used to show a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. Specifically, the kallikrein family includes kallikrein 11 which shares 90% sequence identity with HPAK. More specifically, as shown in Exhibits A and B (submitted in the October 17, 2002 response), SEQ ID NO:1 and kallikrein 11 are **100% identical**

from residues L61-N253 of SEQ ID NO:1. Additionally, Kallikrein 11 has serine protease activity (Exhibit G, pp. 208-9, submitted in the October 17, 2002 response), is a useful marker for distinguishing prostate cancer and benign prostatic hypertrophy and is a potential new biomarker for prostate and ovarian cancer (LocusLink ID 11012; www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=11012, date data viewed, 16, December 2002, Exhibit L, faxed to Examiner Davis, December 17, 2002). Therefore, Applicants' assertion that SEQ ID NO:1 also has serine protease activity would be found by one skilled in the art to be more likely than not true.

Under the applicable law, once the applicant demonstrates a *prima facie* case of homology, the Examiner must accept the assertion of utility to be true unless the Examiner comes forward with evidence showing a person of ordinary skill would doubt the asserted utility could be achieved by a reasonable probability. *See In re Brana*, 51 F.3d at 1566; *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The Examiner has not made such a showing and, as such, the Examiner's rejection should be overturned.

Based on the high level of sequence homology, structural characteristics, subsequent analysis by others showing serine protease activity of TLSP/hippostasin/kallikrein 11 and tissue expression, Applicants have demonstrated a *prima facie* case for homology as an acceptable assertion of utility of the claimed polypeptides. Such an assertion of utility would be determined by one skilled in the art to be more likely than not to be true. Therefore, the Examiner must accept Applicants' demonstration by homology that the claimed polypeptide is a member of the kallikrein polypeptide family and that the homology between the claimed invention and kallikrein polypeptides demonstrates utility by a reasonable probability, unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. The Examiner has failed to make such a showing. Thus, Applicants believe withdrawal of all outstanding rejections is believed to be in order for reasons presented *supra* and in the Response to Office Action submitted October 17, 2002, Supplemental Response to Office Action submitted December 17, 2002 as well as the communication faxed January 13, 2003.

CONCLUSION

In light of the REQUEST FOR CONTINUED EXAMINATION (RCE) request, and the above amendments and remarks, Applicants request Continued Examination of the present application, and request that prosecution be directed to claims to **polypeptides**.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicant's Attorney at (650) 621-8555.

The Commissioner is hereby authorized to charge Deposit Account No. 09-0108 the amount of $750.00 as set forth in the accompanying transmittal letter. If the Commissioner determines that additional fees are due or that an excess fee has been paid, the Patent Office is authorized to debit or credit (respectively) Deposit Account No. **09-0108**.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 21, January 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claim 25 has been canceled.

Claims 1 and 26 have been amended as follows:

1. (**Five Times Amended**) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and

b) a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the sequence of SEQ ID NO:1 over the entire length of SEQ ID NO:1, said polypeptide having serine protease activity.

26. (**Once Amended**) A composition comprising a polypeptide of claim [25] 1 and a suitable pharmaceutical carrier.